Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention

Report of the

Advisory Committee on Childhood Lead Poisoning Prevention

of the Centers for Disease Control and Prevention

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Abbreviations

AAP – American Academy of Pediatrics
ACCLPP – Advisory Committee on Childhood Lead Poisoning Prevention
BLL – Blood Lead Level
CDC – Centers for Disease Control and Prevention
NHANES – National Health and Nutrition Examination Survey
RRP -- Renovation, Repair and Painting Rule

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Executive Summary

Based on a growing body of studies concluding that blood lead levels (BLLs) <10 µg/dL harm children, the Centers for Disease Control and Prevention (CDC) Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) recommends elimination of the use of the term "blood lead level of concern". This recommendation is based on the weight of evidence that includes studies with a large number and diverse group of children with low BLLs and associated IQ deficits. Effects at BLLs < 10 µg/dL are also reported for other behavioral domains, particularly attention-related behaviors and academic achievement. New findings suggest that the adverse health effects of BLLs less than 10 µg/dL in children extend beyond cognitive function to include cardiovascular, immunological, and endocrine effects. Additionally, such effects do not appear to be confined to lower socioeconomic status populations. Therefore, the absence of an identified BLL without deleterious effects combined with the evidence that these effects, in the absence of other interventions, appear to be irreversible, underscores the critical importance of primary prevention.

Primary prevention is a strategy that emphasizes the prevention of lead exposure, rather than a response to exposure after it has taken place. Primary prevention is necessary because the effects of lead appear to be irreversible. In the U.S., this strategy will largely require that children not live in older housing with lead-based paint hazards. Screening children for elevated BLLs and dealing with their housing only when their BLL is already elevated should no longer be acceptable practice.

The purpose of this report is to recommend to the CDC how to shift priorities to implement primary prevention strategies and how to best provide guidance to respond to children with BLLs <10 µg/dL. This report also makes recommendations to other local, state and federal agencies, and the

ACCLPP recommends that CDC work cooperatively with these other stakeholders to provide advice and guidance on the suggested actions.

This report recommends that a reference value based on the 97.5th percentile of the NHANES-generated BLL distribution in children 1-5 years old (currently 5 µg/dL) be used to identify children with elevated BLL. There are approximately 450,000 U.S. children with BLLs above this cut-off value that should trigger lead education, environmental investigations, and additional medical monitoring.

In the pediatric primary care office, primary prevention must start with counseling – even prenatally when possible. This includes recommending environmental assessments for children PRIOR to screening BLLs in children at risk for lead exposure. After confirmatory testing, children at or above the reference value of 5 µg/dL must undergo ongoing monitoring of BLLs. These children should also be assessed for iron deficiency and general nutrition (*e.g.* calcium and vitamin C levels), consistent with American Academy of Pediatrics (AAP) guidelines. Iron-deficient children should be provided with iron supplements. All BLL test results should be communicated to families in a timely and appropriate manner. Children with elevated BLLs will need to be followed over time until the environmental investigations and subsequent responses are complete.

Despite significant progress in reducing geometric mean BLLs in recent decades, racial and income disparities persist. These observed differences can be traced to differences in housing quality, environmental conditions, nutrition, and other factors. The goal of primary prevention is to ensure that all homes become lead-safe and do not contribute to childhood lead exposure. Prevention requires that we reduce environmental exposures from soil, dust, paint and water, before children are exposed to these hazards. Efforts to increase awareness of lead hazards and ameliorative nutritional interventions are also key components of a successful prevention policy.

Historical information on where children with elevated BLLs reside, and other housing data can be used to direct resources for environmental testing and evaluation to homes where lead hazards are more likely to be found. Because lead-based paint hazards are the primary source of childhood exposure to lead in the U.S, and because lead-paint is present in one-third of the nation's dwellings, additional investment is needed to reduce lead hazards in older homes. Housing policies to protect children against lead exposure must target the highest risk properties for priority action, ensure that lead-safe practices are followed during renovation, repair and painting of pre-1978 homes, and to prohibit lead-based paint hazards, including deteriorated paint, in pre-1978 homes.

Local and state government must facilitate data-sharing between health and housing agencies, enact and enforce preventive lead-safe housing standards for rental and owner-occupied housing, help identify financing for lead hazard remediation, and provide families with the information needed to protect their children from hazards in the home.

Additional research is needed to develop and evaluate interventions that effectively maintain BLLs below the reference value in children who reside in pre-1978 housing. Other research priorities should include efforts to improve the use of data from screening programs, develop next-generation point-of-care lead analyzers, and improve the understanding of epigenetic mechanisms of lead action.

Introduction

The Lead Contamination Control Act of 1988 authorized the Centers for Disease Control and Prevention (CDC) to initiate efforts to eliminate childhood lead poisoning in the U.S. As a result, the CDC Childhood Lead Poisoning Prevention Program was created, with primary responsibility to: 1) develop programs and policies to prevent childhood lead poisoning; 2) educate the public and health-care providers about childhood lead poisoning; 3) provide funding to state and local health departments to determine the extent of childhood lead poisoning by screening children for elevated blood lead levels (BLLs), helping to ensure that lead-poisoned infants and children receive medical and environmental follow-up and developing neighborhood-based efforts to prevent childhood lead poisoning; and 4) support research to determine the effectiveness of prevention efforts at federal, state, and local levels.

Furthermore, CDCs Healthy People 2010 initiative set forth as one of its 10-year goals the elimination of childhood lead poisoning. Therefore, CDC, the Department of Housing and Urban Development, the Environmental Protection Agency, and other agencies have developed a federal interagency strategy to achieve this goal by 2010. The key elements of this interagency strategy include: identification and control of lead paint hazards, identification and care for children with elevated blood lead levels, surveillance of elevated BLLs in children to monitor progress; and research to further improve childhood lead poisoning prevention methods.

Advisory Committee On Childhood Lead Poisoning Prevention (ACCLPP)

The Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) was established by the CDC to advise and guide the CDC regarding new scientific knowledge and technical advances and their practical implications for childhood lead poisoning prevention efforts. The overall goal of the ACCLPP is to provide advice that will assist the nation in reducing the incidence and prevalence of

childhood lead poisoning. ACCLPP is charged with evaluating information about the health effects of lead exposure in children, the epidemiology of childhood lead poisoning, implementation issues, and other factors. Furthermore, according to its charter, ACCLPP:

- reviews and reports regularly on childhood lead poisoning prevention practices;
- recommends improvement in national childhood lead poisoning prevention efforts;
- develops written recommendations for the prevention and control of childhood lead poisoning.

Blood Lead Level of Concern Work Group Charge

In keeping with this assignment, ACCLPP established the Blood Lead Level Work Group in November 2010 to recommend a new approach, terminology, and strategy for responding to and preventing elevated BLLs in children. The charge of this working group was to:

- Recommend how to best replace the 'level of concern' in relation to accumulating scientific evidence of adverse effects of BLLs <10 µg/dL in children.
- Consider laboratory capability for measuring BLLs in establishing new guidance on childhood BLLs.
- Advise CDC on how to communicate advisories to groups impacted by policy changes concerning: 1) interpretation of childhood BLLs and trends in childhood BLLs over time; 2) screening and re-screening intervals; 3) requirements and procedures for notifying relevant family members concerning BLL test results; and 4) interventions known to reduce lead exposure.
- Make recommendations for future research on lead-exposure prevention and intervention strategies.

I. Scientific Rationale for Eliminating the CDCs 10 μg/dL Blood Lead Level of Concern

KEY POINTS/RECOMMENDATIONS

- ***Based on the scientific evidence, the ACCLPP recommends that the term "level of concern" be eliminated from all future agency policies, guidance documents, and other CDC publications, and that current recommendations based on the "level of concern" be updated according to the recommendations contained in this report.***

- ***CDC should use a childhood BLL reference value based on the 97.5th percentile of the population BLL in children ages 1-5 (currently 5 μg/dL) to identify children and environments associated with lead-exposure hazards. The reference value should be updated by CDC every four years based on the most recent population based blood lead surveys among children.***

Prior ACCLPP Guidance

The adverse health effects associated with elevated BLLs have been widely studied and documented (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=158823#Download). In the past, the CDC responded to the accumulated evidence of adverse effects of elevated BLLs by lowering the level requiring intervention or what is now deemed the "blood lead level of concern." Over the period from 1960 to 1990, the designated BLL of concern was lowered incrementally from 60 to 25 μg/dL. In 1991, the CDC recommended lowering the BLL for individual intervention to 15 μg/dL, and implementing community-wide primary lead-poisoning prevention activities in areas where many children had BLLs > 10 μg/dL ([1] (http://www.cdc.gov/nceh/lead/publications/>).

In 2005, the ACCLPP again considered the BLL of concern and evaluated new studies that had been published through 2003 relating toxic effects, especially cognitive impairment in children, to BLLs < 10 μg/dL. Based on that evaluation, the CDC issued a statement in 2005[2] (http://www.cdc.gov/nceh/lead/publications/PrevLeadPoisoning.pdf) citing several reasons not to lower the BLL level of concern. These reasons included: 1) the absence of effective clinical or public health interventions identified that could reliably and consistently lower BLLs that were already <10

μg/dL, 2) the assessment that data on IQ in association with BLLs <10 μg/dL relied on fewer than 200 children, 3) the fact that because poor housing, poverty, lead exposure, and cognitive impairment often occurred together especially in the U.S., the role of any specific component in influencing IQ, was difficult to isolate with certainty, and, 4) uncertainties of BLL classification related to laboratory testing precision. The 2005 document also strongly endorsed primary prevention and incorporated these strategies into CDC-funded programs, as well as recommended to other agencies that they act accordingly to carry out primary prevention. In addition, the 2010 Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women [3] (http://www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf) gave the level of 5 μg/dL as the level at which to take action by healthcare and public health providers.

New Evidence and Updating Guidance

However, for multiple reasons, the reliance on both the 10 μg/dL BLL, as well as the concept of a "level of concern" has been increasingly questioned. Since 2003, additional reports of associations between BLLs <10 μg/dL in children with adverse cognitive, and increasingly with other physiological consequences, have been published. Additionally, data from earlier cross-sectional studies of IQ in older children, not considered central to the argument in 2003, have since been re-interpreted as highly relevant, based on reanalysis of prospective data focusing specifically on the time course of associations between blood lead and IQ. The process for setting a "level of concern" for lead has always failed to include consideration of uncertainty or the inclusion of a margin of safety. Although initially intended as a designation of a population-based action level, the level of concern has been widely treated as an individual toxicity threshold. At this time, other countries and even individual U.S. states, have abandoned both 10 μg/dL and the "level of concern."

Consequently, ACCLPP convened a Work Group in 2010 to reconsider the approach, terminology and strategy for elevated BLLs in children. After careful consideration of the current scientific literature, the ACCLPP recommends discontinuation of a designated 'level of concern' for elevated BLL in children. Because no measureable level of blood lead is known to be without deleterious effects, and because once engendered, the effects appear to be irreversible in the absence of any other interventions, public health, environmental and housing policies should encourage prevention of all exposures to lead. Correspondingly, this document emphasizes prevention of exposure rather than responses to specific BLLs, a strategy deemed 'primary prevention.' Public health goals must target the reduction of the disparities in children's BLLs that occur as a result of housing conditions, environmental contamination, race/ethnicity, and socioeconomic status.

As stated in reports from the State of California [5] and Healey et al [4] and, ***a biological "threshold" or "effect level" BLL is not synonymous with a BLL at which intervention is required or effective. Correspondingly, the ACCLPP recognizes that the selection of any BLL as a trigger for action or inaction at an individual or community level will be primarily dependent upon the availability of effective remediation approaches and financial means to accomplish them and, to some degree, related analytical considerations.*** Given those facts, recommendations in the later sections of the document refer to the use of reference values.

A statistically derived reference value characterizes the upper margin of the distribution of the laboratory measurement of a given analyte in a given population. A reference value is useful to characterize individual results as "elevated" or "not elevated" in comparison to the population average or mean value. These values have also been used to set health policy goals and to interpret results from measures of chemical exposure by CDC, the World Health Organization and other

government bodies. The German Federal Environmental Agency has recently applied the use of reference values to define "precautionary action values" for exposures to lead among children and adults [6].

A reference value* is derived from the distribution of concentrations of a specific compound or element in a body fluid of a reference population (often the 97.5th percentile). Therefore, these levels only apply to a specific population at a specific time. In the context of childhood BLLs in the U.S., NHANES data provides an appropriate source for characterizing a reference value for BLLs in children 1-5 years old. We propose that the 97.5th percentile derived from the combination of the two most recent cycles of NHANES data be used to identify individuals with increased exposure and set public health goals. The current reference value (approximately 5 µg/dL) for children's BLLs should be re-considered by the CDC every four years to ensure that changes in this population are adequately assessed.

* The term "reference value" used in this document should be distinguished from the term "reference dose" used by U.S. EPA, which refers to "An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime", or to U.S. EPA's definition of "Reference value (RfV) as "An estimate of an exposure for a given duration to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime" [cf: http://www.epa.gov/iris/help_gloss.htm#r] [accessed 11/09/2011].

Focus on the Weight of Evidence

Section I of this document describes the scientific rationale for the recommendation to eliminate the term "blood lead level of concern." This document is not intended as a risk assessment for lead, nor as a comprehensive review of the current scientific literature. Indeed, the scientific rationale presented here builds upon risk assessments carried out by other regulatory and policy bodies, including the German Human Biomonitoring Commission [6], the State of California [5], and

the literature reviewed in the 2005 CDC statement [2]. Advice on clinical, public health, housing and environmental interventions in relation to BLLs will be described in later sections.

Recognizing that any individual study may have shortcomings, the BLL Work Group based its conclusions on the overall weight-of-the-evidence from epidemiological studies of BLLs <10 μg/dL and the consistency of outcomes. In addition, it considered supporting biological plausibility evidence from animal studies.

Additional Evidence Relating Increasing BLLs with Reductions in IQ

The recommendation of the ACCLPP arises from several considerations. In 2003, Canfield et al. reported decrements in school age IQ among 213 children whose peak BLLs had never exceeded 10 μg/dL [7]. Similarly, Bellinger and Needleman, in a re-analysis of data from 48 children from the Boston cohort study whose BLLs never exceeded 10 μg/dL, reported a similar association [8]. ACCLPP reviewed these and other data, and stated in 2005 that these associations, more likely than not, were causal. There are now additional compelling studies in the scientific literature, reporting associations between BLLs <10 μg/dL and adverse effects in children, forming a more substantive body of evidence than was available at the time of the 2005 CDC statement. Collectively, these new studies and re-interpretation of past studies have demonstrated that it is not possible to determine a threshold below which BLL is not inversely related to IQ.

Healey et al. [4], citing Lanphear et al. [9] as the critical study in its toxicological assessment, asserted that that there is a negative slope relating BLL and IQ down to concurrent BLLs of 1 μg/dL. An increase in concurrent BLL from 1.0 to 4.0 μg/dL is associated with a change in mean IQ of approximately -2.3 to -5.2 IQ points, with a best estimate of -3.7 IQ points. The German Human

Biomonitoring Commission [6] concluded that it is not possible to identify a threshold BLL below which there are no cognitive deficits.

Evidence for Reductions in Academic Achievement and Specific Areas of Cognitive Dysfunction

Studies have also now extended the effects of low BLLs, and suggest the involvement of specific areas of cognitive dysfunction. These include measures of academic achievement such as reading and writing, as well as attention deficits, specifically impulsivity. For example, Chandramouli et al. [10] reported that BLLs in the range 5-10 μg/dL in 30 month-old children were associated with reductions in reading and writing scores in 7-8 year old children from the Avon Longitudinal Study. In a case-control study of children 6-17 years old [11], where the mean BLL was 0.73 and maximum BLL was 2.2 μg/dL, higher BLLs was associated with parent-reported combined-type attention deficit hyperactivity disorder and hyperactivity-impulsivity after controlling for IQ and prenatal smoking.

Significance of the Impact of BLLs on Intelligence

Although only 1 – 4% of the variance in cognitive ability in prospective cohort studies is attributable to lead, the public health impact of low level lead-exposure on the distribution of intelligence in society is considerable. Because exposure to lead is still widespread, it may be responsible for a general reduction in the mean IQ of children. A small change in mean IQ of even 3-5 points associated with BLLs between 1 and 10 μg/dL can shift the entire population IQ distribution, thereby reducing the number of high achieving individuals with IQs above 130, and increasing the number of children with IQ scores below 70, many of whom would need substantial remedial education services [12].

Critical Role of Concurrent BLLs and Intelligence

Studies published since 2005 have also established the importance of concurrent BLLs to IQ reductions. In the U.S., BLLs peak at approximately 2 years of age, after which they decline to lower levels in the absence of specific intervention. Bellinger et al. [13] reported that BLLs measured at 24 months of age, but not at 6, 12, 18 or 57 months of age, were associated with decrements in IQ when measured at 10 years of age in children from the Boston cohort [14]. These findings had cast doubt on any study that did not include data on early childhood BLLs, suggesting that any relationship between BLLs and IQ reductions in large surveys of school age children, such as NHANES, were not causal associations, but rather residual effects of higher BLLs that went unmeasured in early childhood. However, other studies noted that the findings from the Boston cohort appeared to be an exception, as most prospective studies showed stronger associations between concurrent BLLs and IQ reductions at school age, *even though the average BLL at that age was much lower* [15, 16]. In 2005, Chen et al. studied 780 children who qualified for a clinical trial by virtue of having BLLs in the range 20-44 µg/dL when they were "toddlers," and found that lower IQ at age 7 was strongly associated with concurrent BLL, but not associated with peak BLL at 2 years of age [17]. Similar findings were reported in a pooled analysis of major prospective cohort studies of IQ and BLLs, which involved children with and without such high BLLs [9]. Thus, since 2003, data from a much larger number and more diverse group of children with low BLLs and associated IQ deficits have informed consideration of the effect levels. The associations of concurrent BLLs with reduced IQ in this age group suggests a window of developmental vulnerability extending to older children, or perhaps the consequences of protracted exposure during childhood.

Low BLL Effects in Children Extend to Other Organs/Systems

Some recent studies have suggested that the adverse health effects of childhood BLLs <10 μg/dL extend beyond cognitive function to include cardiovascular, immunological, endocrine, and behavioral effects [18-22]. While the data on these outcomes are less extensive than the data characterizing the impact of lead on neurocognitive development, and therefore merit further investigation, they nevertheless raise the possibility that BLLs <10 μg/dL might be associated with broader public health consequences.

Elevated BLL Effects in Children are not Restricted to Low Socioeconomic Status Communities

The conclusions of the 2005 Working Group included concerns for residual confounding by socioeconomic status. It is noteworthy that several studies report associations in populations of relatively "advantaged" socioeconomic status. For example, the analyses from the Boston cohort study, including assessment of children whose BLLs never exceeded 10 μg/dL, was carried out in a "socioeconomically-advantaged population" [8, 13]. Moreover, the BLL-associated reductions in IQ in the Yugoslavian prospective study were seen in Mitrovica, where BLLs were elevated by the local smelter, even though the town also had higher HOME scores and higher maternal IQ scores than the comparison town, Pristina [23]. As pointed out in Healey et al.'s review of 12 longitudinal studies of BLLs and IQ ([4] p. xix), "The pattern of results does not appear to be dependent on cohort demographics, such as SES [socioeconomic status], nor do they appear to be dependent on exposure range – significant associations have been reported among both relatively low and relatively high socioeconomic strata…."

Expectations of Lower BLLs and Changes in IQ and Achievement

It has been argued that even though BLLs have declined, measures on standardized indices such as reading and IQ scores have not correspondingly increased in the U.S., which contradicts the proposed negative association between these measures. As far as the ACCLPP is aware, there are no published data that support this conclusion. Numerous studies have actually reported significant increases in IQ scores over the past century, a phenomenon dubbed the Flynn effect, which has been attributed both to characteristics of the IQ tests themselves and to cultural biases [24, 25]. While this does not demonstrate that lowering BLL is accompanied by higher IQ, it is not incompatible with that possibility. U.S reading scores have increased (http://nces.ed.gov/nationsreportcard/pdf/main2011/2012457.pdf), although to a lesser extent; changes over time are difficult to evaluate given changes in assessment format during this period (National Assessment of Education Progress (NAEP): http://nationsreportcard.gov/ltt_2008/ltt0003.asp and http://nationsreportcard.gov/ltt_2008/ltt0002.asp). (Note however the recent analysis suggesting that the reduction in childhood BLLs in Massachusetts underlies a modest but statistically significant improvement in scores on standardized English and mathematics tests (http://www.bos.frb.org/econoomic/wp/index.htm). Over the same time period, many other significant changes have occurred that could reduce any gains in these cognitive measures, as such functions clearly have multifactorial determinants. For example, the poverty rate has continued to increase (http://www.census.gov/hhes/www/poverty/data/incpovhlth/2010/tables.html), the rates of childhood obesity (http://www.cdc.gov/obesity/data/trends.html#State) and diabetes (http://www.diabetesandenvironment.org/home/incidence/historical) have increased dramatically, and have been associated with cognitive dysfunction [26, 27], and nutritional status has also changed. It is also clear that the U.S. has lost ground in terms of prenatal mortality

(http://www.cdc.gov/omhd/amh/factsheets/infant.htm#1). Moreover, as noted by Healey et al. ([4]p. xxxix): "While the magnitude of the slope of the recommended relationship between mean population IQ and concurrent blood lead in children is undoubtedly influenced to some unknown degree by confounding, it is also likely attenuated by over-control." Other outcomes, such as high school graduation, delinquency, violent crime, or incarceration have a less clear relationship with BLL and perhaps a variable latency. A comprehensive examination of such outcomes might be of interest; however, for reasons of multifactorial determination noted above, it seems unlikely that such effort would yield a consistent interpretation, nor that it would inform judgment about the toxicity of lead at a given BLL.

Shape of the BLL Curve and Outcomes

Other arguments also weigh in this decision. Recognizing the potential for residual confounding, the CDC's 2005 statement ([28]; http://www.cdc.gov/nceh/lead/publications/PrevLeadPoisoning.pdf) explored the question of the steeper dose response at lower BLLs, and evaluated how the interactions among lower dust lead, hand to mouth activity, IQ and BLL might artifactually produce the steeper curve. The document concluded that "Though this hypothetical example cannot demonstrate that residual confounding underlies the steep blood lead-IQ slopes observed at low levels, it does support the need for caution in interpreting the absolute value of the estimated effect sizes." However, it also did not state that the existence of a steeper slope in some data was evidence against any role for lead in cognitive impairment. As such, the specific shape of the curve above vs. below 10 µg/dL is not actually relevant to the question of an association of BLLs with effects below 10 µg/dL. Additionally, for other outcome

measures, effects below 10 μg/dL are found without reports of these effects being of greater magnitude than those above 10 μg/dL.

Uncertainties Regarding the Ability to Reverse Lead Effects in Children

While trials involving chelating agents did not result in improved IQ or behavioral outcomes relative to placebo [29], both human and animal studies have suggested that developmental effects arising from lead exposure could be at least partially ameliorated by opportunities for environmental 'enrichment' [30-33]. The extent to which the developmental impacts of lead-exposure in children can be fully reversed by such strategies as yet remains uncertain. The fact that significant stores of lead are present in bone with a half-life of decades, coupled with the fact that lead can be mobilized from bone back into the bloodstream to maintain equilibrium, if external lead exposure is reduced, makes it difficult to directly test this possibility. Moreover, the prospect that some environmental conditions or host factors (nutritional status, psychosocial stress, etc.) may aggravate the impact of developmental lead exposure has yet to be considered. In general, non-specific interventions that work in Head Start and other enrichment programs might be expected to produce similar results in children with and without a history of elevated BLLs. Tactics aimed solely at lowering BLLs with the expectation of reversing effects, however are unlikely to produce a benefit.

Biological Plausibility Support from Experimental Animal and In Vitro Studies

Finally, the effects reported in children are supported by biological plausibility, i.e., experimental animal studies. Rodent studies have revealed adverse consequences of BLLs of 7-11 μg/dL on cognitive domains comparable to those associated with elevated BLLs in children; these studies have not yet systematically attempted to define clear BLL threshold effects [34, 35].

Moreover, the alterations in the stress response of children in relation to low BLLs [19], particularly the delay in glucocorticoid negative feedback, actually replicates findings in animal models [34, 36].

Animal and *in vitro* studies have identified mechanisms of lead toxicity that could explain the observed greater magnitude of adverse outcomes at lower BLLs for some outcome measures. Reports of non-linear dose effect relationships between BLLs and multiple outcomes, both in human and experimental animal studies, are well established as first detailed by Davis and Svenndsgaard in 1990 [37]. A recent study found a greater delay in post-stress challenge reduction in corticosterone (the rodent version of cortisol) in rats with lower BLLs (maternal exposure yielding peak BLLs of 15-20 μg/dL) than at higher BLLs (30-35 μg/dL) [36].

Furthermore, with respect to the mechanisms of lead effects and possible differential effects at lower rather than higher BLLs, the work of Audesirk and colleagues [38, 39] is highly instructive. Based on a general belief that many effects of lead exposure arise from its ability to substitute for calcium, a metal which is essential to a substantive number of biochemical reactions and physiological processes, this group examined the effects of lead alone or lead plus calcium on the activity of Ca^{2+}/calmodulin-dependent calcineurin. This study demonstrated that lead had the potential, depending upon free concentration of Pb^{2+}, to either stimulate or inhibit Ca^{2+}/calmodulin-dependent calcineurin, with lower lead concentrations increasing and higher lead concentrations decreasing activation of calcineurin.

Summary of Scientific Rationale

In summary, many of the uncertainties associated with effects of BLLs <10 μg/dL cited by the CDC in 2005 [2] have been minimized by more recently published studies. As a result, a BLL without deleterious effects can not be identified at present, and thus the term 'level of concern', or any

suggestion of the existence of a BLL threshold, should be discarded from CDC guidance policies and replaced by new policies and terminology that offer scientifically-based and practical guidance for application in the clinical, laboratory, and public health contexts. Consequently, public health and environmental policies should encourage actions to reduce **all** lead exposure, to the extent feasible [40], and, should specifically focus on minimizing disparities in childhood BLLs as demonstrated by NHANES-documented disparities in housing conditions, environmental contamination, race/ethnicity, and socioeconomic status. Even though the most recent NHANES survey (2007 - 2008) demonstrates considerable progress in lowering BLLs in the U.S., it also confirms that higher BLLs persist in non-Hispanic black children. Similar disparities were noted when BLLs were stratified by poverty-income ratio [41].

A Renewed Call for Primary Prevention

The above arguments as well as those that follow all underscore the critical importance of primary prevention. Using a strategy of identifying lead poisoning or elevated BLL relies on detection in the child, relegating the child to the function of a sensing device for poor/contaminated housing, contaminated water and/or tainted consumer products. Thus, the child can be considered the proverbial 'canary in the coal mine.' The current strategy, which relies on the identifying extant elevated BLLs), while still warranted to some extent, does not prevent the damage already incurred. Moreover, while agents such as chelators can be used to treat overt lead poisoning and possibly reduce the case fatality rate, these agents have been demonstrated not to improve IQ or behavioral consequences of lead exposure. Therefore, primary prevention is the most important and significant strategy.

II. Putting Primary Prevention First

KEY POINTS/RECOMMENDATIONS

- ***CDC should develop and help implement a nationwide primary prevention policy to ensure that no children in the U.S. live or spend significant time in homes, buildings or other environments with lead-exposure hazards.***

Despite the overall reduction in BLLs, each year thousands of children are exposed to lead at levels now associated with negative consequences, including lower academic and life achievement. The evidence supporting this conclusion, some of which is cited in this document, demonstrates that no safe childhood BLL threshold can be identified.

In the past, CDC emphasized primary prevention ([2]; <http://www.cdc.gov/nceh/lead/publications/PrevLeadPoisoning.pdf>), but also recommended screening BLLs in children, to alert policymakers and others to potential lead contamination in communities. Generally, sources of lead exposure were only identified and remediated after a child was identified with an elevated BLL. This strategy should now be considered unacceptable, given that there is no evidence to demonstrate that remediation prevents damage from prior lead exposure [42].

The estimated economic cost of reducing or eliminating lead exposure as well as the predicted associated health benefits are well studied. In most of these analyses, the cost of removing lead contamination was compared to the cost of medical care, special education, and lost productivity; however, more recent analyses often include the benefit of decreased violent crime [43] [44] [45] [46].

The success of regulatory policies that control or eliminate sources of lead in the environment, the lack of proven methods to reverse harm in children with an elevated BLL, and the

lack of a BLL threshold reinforce the need for a primary prevention strategy. CDC defines primary prevention as interventions that reduce or eliminate exposure or risk factors before the onset of disease. They include measures that restrict the use of lead or that remove lead from the environment before exposure occurs. These ideas are not new. In 1970, Dr. Julian Chisolm testified before Congress that 'elimination of the environmental hazard offers the only current practical approach to the prevention of lead poisoning in young children.' [47]. This call for primary prevention to eliminate adverse health effects caused by childhood lead exposure was reiterated by the CDC, in similar language, in multiple documents released after 1975 including guidance documents published in 1991 [48] 2004 [49] and 2005 [2].

Indeed, the success in lowering BLLs reduces the need for programs that chiefly focus on strategies that identity individual lead-exposed children and manage their care, and instead, allows resources to be re-directed to studies of evidenced-based primary prevention strategies. The infrastructure needed to implement an effective primary prevention program is already in place. Over the last 22 years, federal and state agencies have adopted requirements for lead-safe work practices and developed a trained and visible workforce that can safely eliminate lead paint in housing. State and local health and housing programs have used local data to identify geographic areas and sub-populations at high risk for elevated BLLs, as well as specific properties in which many children have been exposed to lead hazards. These data can and should be used to direct lead paint hazard control resources; identify new sources of lead such as traditional pottery or medicines in newly arrived populations; and [anticipate] increased lead exposure, resulting from environmental changes (i.e., alterations in water chemistry that may enhance lead solubility in water).

In summary, the ACCLPP, in concert with elimination of the term "level of concern" for BLLs, recommends that a primary prevention strategy, first proposed in 1970 [47],be implemented to

reduce all environmental exposure to lead. The following sections of this report outline strategies and interventions recommended for achieving this goal.

III. Health Management for Primary Prevention of Lead Exposure

KEY POINTS/RECOMMENDATIONS

- ***Clinicians should be a reliable source of information on lead hazards and take the primary role in educating families about preventing lead exposures. This includes recommending environmental assessments PRIOR to blood lead screening of children at risk for lead exposure.***

- ***Clinicians should monitor the health status of all children with a confirmed BLL ≥5 µg/dL for subsequent increase or decrease in BLL until all recommended environmental investigations and mitigation strategies are complete, and should notify the family of all affected children of BLL test results in a timely and appropriate manner.***

- ***Clinicians should ensure that BLL values at or above the reference value are reported to local and state health and/or housing departments if no mandatory reporting exists and collaborate with these agencies in providing the appropriate services and resources to children and their families.***

Clinicians will play a crucial role in preventing lead exposure and responding to BLLs <10 µg/dL in children, as they are often the primary source of nutritional and lead risk education received by parents. In addition, medical offices are the most common site of childhood BLL testing. Most practicing clinicians have been trained on how to respond to BLLs >10 µg/dL, but with a renewed call for primary prevention and the observed effects of lower BLLs, this section presents a new health management algorithm for children.

Clinicians must be reminded that they have an important role in preventing lead exposure and in managing lead-exposed children. This role should include:

1. Screening questions, outreach and education to minimize exposures prior to blood lead testing;
2. Emphasizing healthy nutrition and/or dietary supplements to reduce absorption;

3. Blood lead testing to promptly identify exposed children, for whom primary prevention has failed;
4. Intervening appropriately when clinically indicated;
5. Overseeing ongoing monitoring of children with elevated BLLs, defined as levels above the reference value;
6. Coordinating efforts with parents and local and state authorities to minimize risks to individual children and to assist communities in their primary prevention efforts.

Exposure Prevention; Role of the Clinician

Clinicians should be a consistent and reliable source of information, and take a primary role in educating families about the risks of lead-exposure. If appropriately educated, all families will be better equipped to make sound housing decisions based on an understanding of the risks associated with lead hazards. Anticipatory guidance for parents should cover a number of lead risk topics, including: in-home exposures; unsafe renovation practices; and potential lead-exposures associated with parental occupations and hobbies. Parents should receive information on identifying lead hazards and safe/reliable methods to minimize exposures, as well as contact information for additional local lead-related resources. In addition, the clinician has a role in recognizing risks from potential lead exposures specific to immigrant communities, refugees and children adopted from foreign countries, whose previous and/or ongoing lead exposure may include folk/home remedies, medications, toys, cosmetics, food, ceramic ware, and other less common items.

Personal Lead Risk Assessment Questionnaires

The effectiveness of personal risk assessment questionnaires for identifying children with elevated BLLs has been documented [50]. However, no studies have evaluated the performance of

these questionnaires at BLLS <10 μg/dL or their effectiveness in directing counseling or in identifying lead hazards in the home. When applied in consecutive samples of patients in clinical settings, the ability of such questionnaires to identify children with BLLs ≥10 μg/dL varies considerably by population [50]. In certain studies, sensitivity was better for higher BLLs [51] or when questionnaires were developed for specific populations [52] [53]. In general, to identify approximately 80% of children with BLLs ≥10 μg/dL, a blood test was required in 50% of those assessed using a questionnaire. Multiple studies in populations with low [52] or high [54, 55] prevalence of elevated BLLs concluded that risk assessment questionnaires were not effective in a clinical setting. When screening, it is important to keep in mind that exposure may begin *in utero*; thus, potential exposures during pregnancy should be considered (Table 1). In addition, it should be noted that young children may be exposed to lead through contact with paint, water, dust, and soil [56].

Minimizing Absorption

In their role as advocates for children's health and as educators of parents, clinicians routinely provide nutritional guidance. A well-balanced diet is essential to meeting the child's recommended daily allowance of essential vitamins and minerals and to provide adequate calories for growth. Certain vitamins and minerals, especially calcium, iron and vitamin C, play a specific role in minimizing lead absorption. Regular assessment of the child's nutritional status during well-child care can identify children with inadequate intake of these and other nutrients, and allow the clinician to proactively recommend supplementation. Note that the Committee on Nutrition of the American Academy of Pediatrics recently published a comprehensive review of the diagnosis and prevention of iron-deficiency and anemia ([57]; <http://pediatrics.aappublications.org/content/126/5/1040.full.html>).

For the potentially lead-exposed child, adequate intake of iron, calcium and vitamin C, beyond their requirement for overall good nutrition, can specifically minimize absorption of ingested lead. For children with BLLs above the reference value, it is imperative to further reinforce healthy eating habits and reinforce nutritional education. It is reasonably well-established that iron deficiency is associated with increased BLLs, and that some effects, such as lower IQ, can result from both conditions. Thus, children at high risk of lead exposure should be tested for iron deficiency and iron-deficiency anemia and treated according to current AAP guidelines.

Specific assessment of bodily iron stores can be an essential part of treating lead-exposed patients, because iron-deficiency anemia results in increased intestinal absorption of ingested lead [58, 59].

Table 1. Risk Factors for Lead Exposure in Pregnant and Lactating Women

√	**Recent immigration from or residency in areas where ambient lead contamination is high.** Women from countries where leaded gasoline is still being used (or was recently phased-out) or where industrial emissions are not well-controlled.
√	**Living near a point source of lead**, such as lead mines, smelters, or battery recycling plants (even if the establishment is closed).
√	**Working with lead or living with someone who does**. Women who work in or who have family members who work in lead-industry (take home exposures).
√	**Using lead-glazed ceramic pottery**. Women who cook, store, or serve food in lead-glazed ceramic pottery made in a traditional process and usually imported by individuals outside the normal commercial channels.
√	**Eating non-food substances (pica)**. Women who eat or mouth non-food items that may be contaminated with lead (such as soil or lead-glazed ceramic pottery)
√	**Using alternative or complementary medicines, herbs, or therapies**. Women who use imported home remedies or certain traditional herbs that may be contaminated with lead
√	**Using imported cosmetics or certain food products**. Women who use imported cosmetics, such as kohl or surma, or certain imported foods or spices that may be contaminated with lead.
√	**Engaging in certain high-risk hobbies or recreational activities**. Women who engage in high-risk activities or have family members who do.
√	**Renovating or remodeling older homes without lead hazard controls in place**. Women who have been disturbing lead paint and/or creating lead dust, or spending time in such a home environment.
√	**Consumption of lead-contaminated drinking water**. Women whose homes have leaded pipes or source lines with lead.
√	**Having a history of previous lead exposure or evidence of elevated body burden of lead**. Women who may have high body burdens of lead from past exposures, particularly those who are deficient in certain key nutrients (calcium, iron).
√	**Living with someone identified with an elevated lead level**. Women who may have exposures in common with a child, close friend, or other relative living in same environment.

Formerly, hemoglobin (Hgb) screening was recommended, however Hgb alone is only sufficient to diagnose anemia (by definition), and does not specifically rule out iron deficiency. Iron deficiency, defined as inadequate bodily iron stores to preserve function, may be present without anemia. In order to sufficiently assess iron status, iron levels, total iron binding capacity (TIBC) or serum ferritin (SF) can be used. An abnormal value on any test can be diagnostic of iron deficiency. Children identified as iron deficient should be treated with an appropriately dosed iron supplement,

and reassessed periodically during treatment. Clinicians must keep in mind the risk of toxicity associated with excess iron intake [57]and counsel parents accordingly.

Evaluation and Treatment of Lead Exposure - Identifying Exposed Children

A national surveillance program is crucial to gauge the success of our public health programs, identifying subpopulations with higher exposure, and determining the reference value. In addition, clinical testing for lead exposure must continue for the foreseeable future in order to identify those children for whom primary prevention measures have failed.

BLL testing is currently required at 12 and 24 months for all Medicaid-enrolled children, regardless of known lead-exposure risk. Testing will often occur during routine well-child care as recommended by the American Academy of Family Physicians and the AAP. In addition, children ≤72 months who missed recommended screening at a younger age should be screened at presentation. Screening at 12 and 24 months satisfies the Healthcare Effectiveness Data and Information Set (HEDIS) measures. However, it is important to perform at least one BLL in all children between the ages of 12-24 months, regardless of insurance status, to obtain accurate measurements of population BLL.

In 1991, CDC recommended universal BLL testing for all children, with different screening requirements for ≥6 month old children at low and high risk of lead-exposure [48]. In 1997, the CDC recommended that state and/or local agencies formulate their own lead screening recommendations based on local data, because of the wide variability in lead-exposure in different urban and rural U.S. communities [60]. In particular, the CDC recommended universal lead screening for communities with a ≥27% pre-1950 housing or ≥12% prevalence of ≥10 μg/dL blood lead in children 12-36 months old. They further, recommended targeted screening for specific groups with higher risk factors in communities with lower prevalence of elevated BLLs. In the absence of a statewide or local plan,

universal BLL testing according to the 1991 CDC guidance is recommended. Based on the prevalence of elevated BLLs, local health departments or other relevant agencies may implement different testing guidelines, such as screening more frequently or at different ages. However, CDC and Medicaid are currently negotiating the criteria for local exemptions. In general, information about CDC-approved local screening programs can be found at: http://www.cdc.gov/HealthyHomes/programs.html.

A 2005 guidance statement from the AAP summarized the history of lead screening and suggested that pediatricians screen according to local and state guidelines where they apply, but screen all non-Medicaid children in their absence, and also screen all immigrant, refugee and internationally-adopted children when they arrive in the U.S., due to their increased risk [61]. The numerous reports of children with high blood lead levels, including fatalities, in many countries, as well as lead exposure from imported products support the screening of foreign-born children [62-65] [66]. The CDC also recommends initial and follow-up screening of pregnant and lactating women [3], as well as for neonates and infants of women with BLLs ≥5 µg/dL.

ACCLPP recommends that health care providers follow local and state lead screening guidelines, screen children coming from other countries when they arrive in the United States, and screen neonates and infants born to women with lead exposure during pregnancy and lactation per earlier CDC guidance. It recommends that children be screened according to guidelines for Medicaid-enrolled children and the 1997 CDC guidelines for jurisdictions (screen at ages 12 and 24 months, and once between 36 to 72 months of age in those without prior screening) in jurisdictions without formal recommendations until those recommendations are issued. (See reference [40] for more detail.)

Some communities may provide screening outside of the child's medical home (such as through the WIC program). It is not necessary for the clinician to duplicate those efforts, but he/she should confirm that the screening was performed elsewhere before testing is deferred during the office visit.

Evaluation and Intervention Strategies for Children with BLLs above the Reference Value

With the move away from a designated "level of concern," a new algorithm is needed to provide clinicians with guidance on responding appropriately to the lower range of BLLs. It is now clear that there is no known threshold below which adverse effects of lead are absent. Management strategies for children whose blood levels are equal to or greater than the reference value include nutritional education and intervention, if indicated, educational intervention, ongoing monitoring, and coordination with other organizations (Table 2).

Coordination of care with the local authorities and organizations, including local Childhood Lead Poisoning Prevention programs is essential to initiate prompt investigation for the source of lead exposure and potentially plan a response strategy. Although these services are typically outside of the clinician's role, medical and environmental interventions should be implemented simultaneously to best protect the child. In addition, families with children whose BLLs are above the reference value should be given access to services that provide:

1. Education about existing codes, lead-safe housing rules, disclosure requirements, landlord responsibilities, risk factors for lead exposure in the home and at work, and steps for maintaining a lead safe home (lead hazard identification and repair, lead dust testing, EPA and state Renovation, Repair and Painting (RRP) requirements, and do-it-yourself precautions)

2. Home visits by CLPPP staff, community health workers, Maternal and Child Health home visiting programs, and other systems to assess the home, advise occupants, report observations and lead test results, and make referrals in response to identified lead hazards.
3. Assistance and guidance regarding landlord violations of RRP, other lead rules, and housing codes, including legal services for egregious situations like evictions and serial offender property owners and referrals to code enforcement.
4. Educational needs of children with BLLs above the reference value are being addressed in a separate publication from the ACCLPP.

Communicating BLL Test Results

Effective screening policies and practices should ensure that the children of high-risk families (i.e., families on Medicaid), are screened, and that lead-exposed children or children with elevated BLLs receive key environmental interventions and case management services. Funding to sustain these activities is an essential building block. Interactions with affected families must be performed in a culturally-sensitive, same-language, and streamlined manner. The medical home, laboratory, and other providers should offer simple information about the meaning of elevated BLL test results and relevant, culturally-sensitive messages about relative impact should be conveyed. Specialized terms such as detectable level or elevated BLL should be defined. Pediatricians and other providers shall integrate BLL test results into the "basic" report of indicators like weight, height, and developmental percentiles. Pediatricians commonly present data in the form of percentiles, and a similar convention could help physicians explain elevated BLLs to parents. (See reference [40] for more information, and [67] for patient handouts). Test results should not be mysterious or difficult to obtain; parents should

have continuous access to BLL test results via internet and telephone retrieval systems until the child reaches the age of twelve.

Pediatricians should explain the uncertainty of all quantitative medical tests and BLL testing. In particular, testing capillary blood for lead may be affected by residual lead contamination ingrained on children's fingers, and that can be very difficult to remove. Thus, a capillary blood lead test above the reference value should be repeated using a venous blood sample. Even in the best laboratories, variations in test results of ±2 μg/dL are normal and are well within the acceptable lab error. Multiple BLL tests are needed over time to examine true trends in actual blood lead levels . (See reference [40] for more detailed discussion).

Given the challenges involved in measuring BLLs as low as 5 μg/dL, quality assurance practices will need to be updated with the goal of improving accuracy and repeatability of BLL testing. ACCLPP previously recommended that the federal Centers for Medicare & Medicaid Services, which is responsible for regulating clinical laboratory testing through the Clinical Laboratory Improvement Amendments 1988 [68, 69], move as soon as possible to revise current regulations for allowable laboratory error permitted in blood lead proficiency testing programs from ±4 μg/dL to ±2 μg/dL for BLLs ≤ 20 μg/dL. Additional adjustments to internal laboratory quality assurance procedures may be warranted, especially at BLLs <10 μg/dL. Laboratory practices and associated recommendations are being addressed in a separate publication.

Confirmatory Testing of Children with BLLs above the Reference Value

Given the uncertainty of individual blood lead test results, it is important to do confirmatory testing, especially for capillary blood samples that might be elevated due to residual lead on the skin

at the puncture site. The recommended schedule for confirmatory testing is summarized in Table 3 and includes:

1) All capillary and venous BLL results greater than or equal to the reference value must be confirmed within 1-3 months;

2) Children with BLLs ≥45 µg/dL or with symptoms of lead poisoning should have an immediate (within 48 hr) confirmatory test;

3) Response actions should be initiated only after elevated BLLs are confirmed.

Management of Children with BLLs above the Reference Value

No changes are recommended to the existing CDC guidelines for the evaluation and treatment of children requiring chelation (those with BLLs ≥ 45 µg/dL) [70]. Unless the clinician is intimately familiar with treatment protocols, he/she should consult with a medical toxicologist and/or regional Pediatric Environmental Specialty Health Unit (PESHU), or a clinician experienced in treating children with elevated BLLs. Contact information for regional PESHUs can be obtained at http://aoec.org/PEHSU/serviceareas.htmlhttp://aoec.org/PEHSU/serviceareas.html; local or regional poison control contact information is available at http://npic.orst.edu/health/poison.htm.http://npic.orst.edu/health/poison.htm. The CDC's Lead Poisoning Branch is another resource available to clinicians at http://www.cdc.gov/nceh/lead/about/program.htm.http://www.cdc.gov/nceh/lead/about/program.htm. Children who undergo chelation should be monitored at least monthly, if not more often, for potential side effects.

Of note, there are numerous touted interventions that are, at best, unnecessary and dangerous, and, at worst, can be fatal. Non-medically managed chelation therapy has been widely promoted in

lay literature and on the internet as a cure for a variety of diseases and disorders. These claims are not scientifically-based, and families should be counseled proactively against becoming a victim of these unproven and sometimes dangerous treatments. There is no medical foundation for relying on the following methods to diagnose over-exposure to lead: gingival lead lines, testing of neurophysiologic function; evaluation of renal function (except during chelation with EDTA); testing of hair, teeth, packed red cells, saliva or fingernails for lead; radiographic imaging of long bones (see reference [70], Chapter 3) nor is provocative chelation prior to measurement of lead in urine testing recommended. The widely accepted sequelae of BLLs <45 µg/dL are cognitive and behavioral impairment. Chelation of children with BLLs ≥ 20 and ≤45 µg/dL has not been shown to offer therapeutic benefit for these outcomes [29].

Ongoing Monitoring For Lead-Exposed Children

For the child identified with a BLL results greater than or equal to the reference value, ongoing monitoring of BLL is indicated during and after appropriate medical, educational and environmental interventions (See Table 4). BLLs that rise may be indicative of an unrecognized source of exposure, inappropriate abatement activities, failure to mitigate the identified hazard, or the redistribution of lead stores within the child's body. For the child with a rising BLL, additional medical and environmental evaluation and interventions may be necessary, along with ongoing coordination of care with the local CLPP. This monitoring is essential to identify a given source of lead, help determine if there is any ongoing exposure, and to verify the decline in BLL after lead sources have been reduced or eliminated. Ongoing monitoring is also essential for children undergoing chelation [61, 70, 71].

Table 2: Recommended actions based on BLL

<Reference Value	≥Reference Value ≤45	≥45 ≤69	≥70
Lead education -Dietary -Environmental Environmental assessment* for pre -1978 housing Follow-up blood lead monitoring (see pages 23 - 24)	Lead education -Dietary -Environmental Follow-up blood lead monitoring Complete history and physical exam Lab work: - Iron status Consider Hemoglobin or hematocrit Environmental investigation Lead hazard reduction Neurodevelopmental monitoring - Abdominal X-ray (if particulate lead ingestion is suspected) with bowel decontamination if indicated	Lead education -Dietary - Environmental Follow-up blood lead monitoring Complete history and physical exam Lab work: -Hemoglobin or hematocrit -Iron status -Free erythrocyte protoporphyrin Environmental investigation Lead hazard reduction Neurodevelopmental monitoring Abdominal X-ray with bowel decontamination if indicated Oral Chelation therapy Consider hospitalization if lead-safe environment cannot be assured	Hospitalize and commence chelation therapy (following confirmatory venous blood lead test) in conjunction with consultation from a medical toxicologist or a pediatric environmental health specialty unit Proceed according to actions for 45-69 μg/dL

* The scope of an "environmental assessment" will vary based on local resources and site conditions. However, this would include at a minimum a visual assessment of paint and housing conditions, but may also include testing of paint, soil, dust, and water and other lead sources discussed previously, e.g., [56]. This may also include looking for exposure from imported cosmetics, folk remedies, pottery, food, toys, etc. which may be more important with low level lead exposure. See Section V for further clarification.

Table 3. Recommended Schedule for Obtaining a Confirmatory Venous Sample

Blood µg/dl	Time to confirmation testing
≥ Reference Value- 9	1 - 3 months
10-44	1 week – 1 month *
45-59	48 hours
60-69	24 hours
≥70	Urgently as emergency test

* The higher the BLL on the screening test, the more urgent the need for confirmatory testing.
(Adapted from: *Screening Young Children for Lead Poisoning: Guidance for State and Local Public Health Officials. Atlanta: CDC; 1997.)*

Table 4. Schedule for Follow-Up Blood Lead Testing[a]

Venous Blood lead level µg/dl	Early follow up testing (2-4 tests after identification)	Later follow up testing after blood lead level declining
≥ Reference Value – 9	3 months *	6-9 months
10 - 19	1-3 months *	3-6 months
20 - 24	1-3 months *	1-3 months
25 - 44	2 weeks- 1 month	1 months
≥45	As soon as possible	As soon as possible

[a] Seasonal variation of BLLs exists and may be more apparent in colder climate areas. Greater exposure in the summer months may necessitate more frequent follow ups.

* Some case managers or PCPs may choose to repeat blood lead tests on all new patients within a month to ensure that their BLL level is not rising more quickly than anticipated.

Children Deserving Special Attention

Numerous publications highlight the lead exposure risks to children from some immigrant communities arising from a wide range of ongoing exposure sources or from exposures in their country of origin. These children are at greater risk of having a BLL above the reference value outside of the typical age range targeted for testing. Therefore, it is recommended that all immigrant children, including international adoptees, be tested for lead exposure, with home evaluation to identify sources if indicated.

Developmentally-delayed children with hand-to-mouth behavior persisting beyond the typical age range should also be considered candidates for continued monitoring. In addition, healthcare providers should consider blood lead testing for siblings of children with BLLs above the reference value given the potential for lead exposure.

IV. Achieving Lead-Safe Housing

KEY POINTS/RECOMMENDATIONS

- ***Educate families, service providers, advocates, and public officials on primary prevention of lead exposure in homes and other child-occupied facilities, so that lead hazards are eliminated before children are exposed.***

- ***CDC should encourage local, state, and other federal agencies to: 1) facilitate data-sharing between health and housing agencies; 2) develop and enforce preventive lead-safe housing standards for rental and owner-occupied housing; 3) identify financing for lead hazard remediation; and 4) provide families with the information needed to protect their children from hazards in the home.***

ACCLPP has stated previously that the recommended approach to prevent lead poisoning is to reduce exposures to lead-based paint hazards and to make and keep the U.S. housing stock "lead-safe". The most common sources of exposure among children with BLLs above the reference value are lead hazards in and around older housing, including deteriorated lead-based paint, lead-contaminated dust, and accessible lead contaminated soil. Approximately 35% of all U.S. housing units have some

lead-based paint, and 22% have significant lead-based paint hazards [72]. Low income households are more likely to live in a home with lead-based paint hazards (29%) than higher income households (18%) [72].

Controlling and Preventing Lead Based Paint Hazards

Property owners can correct deteriorated paint and other lead hazards in the home environment. Some local and state laws require abatement in a home where a child has been lead-poisoned; this specialized work must be done by a certified abatement contractor. Abatement involves permanent elimination of hazards through methods, such as enclosure, encapsulation, and paint removal proven to last at least for 20 years. Interim controls and other lead-safe paint repairs do not "permanently" eliminate hazards, because the paint is still present, but are effective in arresting paint deterioration, if the underlying cause is addressed.

Uncontrolled renovation and painting that disturbs painted surfaces and generates leaded dust and debris is a common route of child exposure to lead in the home. The events can occur wherever there is lead-based paint, regardless of the condition of the building's painted surfaces. In some communities, one-third to one-half of childhood lead poisonings have been reportedly derived from renovation work. EPAs RRP rule now requires the use of trained, certified renovators for activities that disturb painted surfaces in pre-1978 homes and child-occupied facilities. Twelve States are authorized by EPA to conduct RRP in their jurisdictions. These states and EPA have certified 600,000 trained renovators. Maintaining paint in intact condition is the key strategy for preventing deteriorated paint; fixing leaks can be an important means to this end. Although peeling paint is a violation of most local and state housing codes, some officials are not aware of the importance of citing the problem.

Policies to Advance Lead Safe Housing

Primary prevention strategies focused on housing must be calibrated to address geographic variation in the risk for lead exposure and to suit local circumstances, needs, and assets. Communities and homes at highest risk should receive the greatest attention and resources. Collaboration among housing, community development, and code enforcement agencies, property owners, and community-based organizations is essential, in order to prioritize housing where occupants are likely to be at greatest risk.

Effective implementation of primary prevention requires access to a continuum of different strategies for improving lead safety in various niches of the housing stock, with the goal of zero tolerance for lead hazards. Key agencies must understand their roles and opportunities to stop lead poisoning, particularly in code enforcement and repair financing. Lead-safe housing laws and ordinances and housing or sanitary codes provide objective standards against which landlords can demonstrate compliance. Property owners must ensure that deteriorated paint is repaired and not create new hazards in the process. Renovators must comply with RRP and be held accountable to "do no harm" throughout the repair and painting process. Ideally, code agencies should be authorized to cite non-compliance with RRP. Every effort should be made to integrate lead safety into other housing activities, and to train and educate families, service providers, advocates, and public officials to advance primary prevention by addressing lead exposure before a child is poisoned.

Because peeling paint and building materials in disrepair are already code violations in many jurisdictions, enforcing these requirements is the basic minimum lead-safe housing policy. Federal and state RRP mandates that paint repair activities in pre-1978 homes adhere to lead-safe work practices designed to contain, control, and cleanup lead dust and debris. Because lead dust is

invisible, clearance dust testing should be required after ordered repairs and in high-risk situations to be certain that lead-contaminated dust does not remain behind to poison a child.

Recommendations for Local and State Government

Elected officials and the leaders of health, housing, and code agencies can help to protect their jurisdictions' children from lead in their homes through many activities [28, 73, 74] including these six strategic approaches:

A. **Target actions in pre-1978 properties according to known risk factors since the extent of risk varies from property to property.** Jurisdictions can have policies for designating higher risk properties and specifying safeguards such as priority enforcement, environmental testing requirements, more protective interventions such as abatement and interim controls, and higher penalties for violations and non-compliance in response to risk. Multiple criteria can be combined to best meet local needs. The key risk factors that should trigger additional requirements and priority enforcement include real estate transactions (property sale, re-rental, or remodeling), housing age (i.e. built before 1940/1950/1960), poor property condition, housing code or environmental violations, and reported presence of lead hazards. Of course units and properties occupied by children with blood test results above the CDC's reference value should be targeted if not reached by other environmental intervention policies. Neighborhood-level risk factors include socioeconomic factors such as household income level, race/ethnicity and other neighborhood demographics, concentrations of code violations, and other issues that can be tracked using census or local agency data.

B. **Establish institutional linkages between public health programs and housing code enforcement agencies to prioritize rental properties based on previous code violations and reported blood**

lead levels above the reference value. These agencies must share data to uncover lead hazards and confront housing violations of mutual concern, while independently fulfilling their respective responsibilities for taking action.

C. Enact preventive housing standards and policies for rental housing (multifamily and single-family) that mandate:

1. Property owner maintenance of painted surfaces and for other building components and systems, and verification with an annual visual inspection for signs of water damage, moisture problems, and deteriorated paint. Such inspections should also be mandated at unit turnover.
2. Proactive and routine code inspections that enable the code official to check all rental dwellings for problems.
3. Priority enforcement of code requirements for intact paint in pre-1978 homes. To ensure no lead dust hazards remain after ordered repairs, the property owner should obtain clearance testing, and the agency that ordered repairs should confirm that the repairs were completed.
4. Attention to lead hazards at unit turnover since the convenience of current occupants is not of concern in a vacant unit.
5. Clearance testing and a visual inspection to ensure that the home is lead-safe prior to renting to new tenants and after other real estate transactions affecting rentals such as property sale, lease renewal and refinancing.
6. Visual inspection and clearance dust testing after RRP jobs to ensure no lead dust hazards remain.
7. Disclosure to other occupants, environmental testing, and building-wide repair if one unit in a multifamily property has exposed a child to too much lead or contains lead hazards, since there is a significant likelihood that similar hazards are present in other units in the building,

due to the common construction, painting, and maintenance history. Other units' tenants can take steps to protect their children from lead exposure and have their children screened for lead if they receive this information.

D. Enact preventive housing standards and policies for owner-occupied housing. While enforcement opportunities for preventive housing standards and policies in these properties are more limited, jurisdictions can mandate the following**:**

1. Priority enforcement of maintenance standards for painted surfaces and other building components and systems on the exterior of an owner-occupied property. Citation of these conditions can be reasonable cause for an interior inspection if there are indications of other risk factors. To ensure no lead dust hazards remain after ordered repairs, the owner-occupant should obtain clearance dust testing, and the agency that ordered repairs should confirm that the repairs were completed.
2. Property owner performance of a visual inspection for signs of water damage, moisture problems, and deteriorated paint prior to sale.
3. Disclosure to other multifamily occupants if a child with a BLL above reference value is identified in any unit, since there is a significant likelihood that similar hazards are present in other units in the building or complex, due to common construction, painting, and maintenance history. After property management provides this information, the other occupants, can take steps to protect their children from lead poisoning and have their children screened for lead.
4. Visual inspection and clearance dust testing after RRP jobs to ensure no lead dust hazards remain.

E. Provide Loans, Grants, and Other Financial Incentives for Hazard Remediation

Jurisdictions and financial institutions should assist property owners in obtaining financial assistance to remediate lead hazards. HUD's Lead Hazard Control Program Grants assist 300 homes in 30-50 communities each year. Jurisdictions that receive a formula allocation of Community Development Block Grant (CDBG) and HOME funds have broad discretion in using these block grants for a wide range of purposes, including housing rehabilitation and lead hazard control, according to their Consolidated Plan, and should ensure that available data on lead poisoning is taken into account in setting priorities. Private lenders offer loans on their own initiative, as well as under federal programs like FHA's 203(k) buy-rehab program, HUD's Title 1 program, and USDA's Rural Housing Administration programs, and in response to requirements under the Community Reinvestment Act. To advance the availability of financial assistance, jurisdictions should seek prioritization of lead remediation through set-asides and favorable financing terms, encourage financial institutions to make strategic investments in lead remediation, and promote the adoption of tax credits for this purpose. Because intervention investments will have more durable results if they improve each unit across the spectrum of environmental health and energy-efficiency, multi-purpose funding is needed to leverage categorical programs, and public officials should require effective inter-agency coordination to optimize repairs in the same home by various funding streams.

F. Assist Families in Taking Self-Protective Actions

Parents and caregivers in all families who live in pre-1978 buildings, and especially families living in high risk housing need effective direction and supportive services to protect their children.

Implementation of primary prevention requires that all families know how to protect their own children from lead exposure in their own homes. Every effort should be made to train and educate families in basic tactics in maintenance, and in communications with landlords, contractors,

and others who can influence the presence of lead hazards in their homes. Service providers who are in the home or otherwise in communication with high-risk families can help through observation, education, advocacy and referrals.

V. Environmental Interventions

KEY POINTS/RECOMMENDATIONS

- ***CDC should emphasize the importance of environmental assessments to identify and mitigate lead hazards before children demonstrate BLLs above the reference value. Prevention strategies must be adopted to reduce environmental exposures from lead in soil, dust, paint and water before children are exposed.***

- ***If lead hazards trigger a response in any unit in a multi-family housing complex, the same response action should be applied to all similar untested units in the housing complex, unless a risk assessment demonstrates that no lead hazards are present in the other units.***

The goal of primary prevention is that all homes will become lead-safe and not contribute to childhood lead exposure. Given the involuntary nature of lead exposures associated with housing and other sources, and the risks associated with lead exposure, all exposures should be kept as low as possible. Controlling potential lead exposures in a child's environment before they cause damage will be the only way to prevent childhood lead poisoning. Special vigilance is also needed around renovation and remodeling activities in older homes, when lead dust levels are known to spike.

Lead-contaminated dust, soil, paint, and water are all associated with blood lead levels above the reference value in children, as are other risk factors, such as parent's occupation, age of housing, poverty and ethnicity. Although most published research associating environmental lead exposures and BLLs for children was done with children who had significantly higher levels than is common today, there are notable exceptions, such as the recent NHANES analyses of dust and children's BLLs [75, 76].

Multiple risk factors/ exposures contribute to BLLs less than 10 µg/dL. In fact investigations conducted in response to a child with a BLL greater than 15 µg/dL often fail to identify a single source or risk factor and the challenge is even greater for lower level exposures. The inability to identify a single source of exposure in these cases underlines the fact that lead remains a multi-media pollutant requiring integrated exposure assessment and reduction. However in the U.S., lead-based paint hazards, including deteriorated paint, and lead-contaminated dust and soil still remain by far the largest contributors to childhood lead exposure on a population basis [56].

Although the U.S. Environmental Protection Agency has established recommended lead exposure limits for dust, soil, and water in homes, these levels are not health based and were not selected to be protective of exposures below 10 µg/dL. For example, the current hazard standard for dust lead levels for floors of 40 $\mu g/ft^2$ is associated with potential exposures among children above the reference value. Recent analysis of NHANES blood and dust lead data, for example, indicates that when floor dust lead is less than 12 $\mu g/ft^2$, the geometric mean BLL is 3.9 µg/dL [75, 76]. Water and dust lead levels are currently under review by EPA. (See http://yosemite.epa.gov/sab/sabproduct.nsf/RSSRecentHappeningsBOARD/9c733206a5d642578525 7695004f0cb1!OpenDocument&TableRow=2.2 and http://water.epa.gov/lawsregs/rulesregs/sdwa/lcr/index.cfm#LongTermRevisions

A successful primary prevention strategy must start with an environmental assessment in order to set priorities and inform the selection of appropriate response actions. Environmental inspections and testing are also necessary responses to cases where a child has already been exposed (See Table 2).

Significant research on children with BLLs greater than 25 µg/dL has focused on the efficacy of a range of lead hazard controls and abatement of lead hazards (including dust, soil, and paint) and in

uncontrolled trials has shown statistically significant declines in BLLs in the range of 20-30 percent at follow up (reference [70] p. 95). Only very limited research has examined the efficacy of lead abatement techniques and interim controls for children with BLLs as low as 5-9 μg/dL [77]. Evaluation of the decline in BLLs following environmental interventions is problematic because bone lead stores may remain a significant contributor to BLLs for many years following removal from further exposure and/or chelation.

As we pursue and prioritize a primary prevention model, we move beyond the goal of interventions just aimed at lowering a child's BLL. The new emphasis must be on efforts that are successful at reducing exposures to known sources. Prevention requires that we reduce environmental exposures from soil, dust, paint and water before it contributes to a child's exposure. Because blood lead integrates all sources of exposure including lead released from bone stores, it should not be used as a sole measure to determine whether or not a specific environmental exposure has been successfully addressed. Instead, environmental measurements, e.g., soil, or dust testing, are a more direct and preferred means of assessing whether an intervention has succeeded.

Environmental testing is a useful means to focus limited hazard control resources. Environmental testing protocols have now been standardized and trained professionals who are either certified or licensed are available to carry them out ([78]; <http://portal.hud.gov/hudportal/HUD?src=/program_offices/healthy_homes/lbp/hudguidelines) ([79]; <http://portal.hud.gov/hudportal/documents/huddoc?id=DOC_19537.pdf>).

Observations by health departments and peer-reviewed studies have indicated that specific addresses are often linked to repeated cases of elevated BLLs in children. For example, in Jefferson County, Kentucky, 79 homes housed 35% of the 524 cases identified in one five-year period [80]. Another study showed that neighborhoods based on census tracts predict rates of elevated BLLs

among children [81]. In one study, lead hazard controls employed in select units significantly reduced the likelihood of another child being lead poisoned compared to units where hazards were not reduced[44]. Rental status, along with other housing characteristics, is also a predictor of BLLs greater than 10 µg/dL [9]. ***Such information can be used to focus resources for environmental testing and evaluation on homes where lead hazards are more likely to be found.***

Environmental investigations in housing built before 1978 should include:

- History of child's exposure and questionnaire on potential sources of exposure;
- Visual inspection of the home or facility where the child spends considerable time to identify peeling paint, moisture damage, and other relevant housing conditions;
- Measurements of lead levels in dust (with single surfaces wipe samples), soil, water, and paint that is not intact or otherwise separating from the substrate should be conducted.

Environmental assessments in response to children with elevated BLLs are also appropriate in homes built after 1978 when the use of lead paint was restricted. In one large national survey three percent of homes built from 1978-1998 had lead-based paint hazards [82]. However, the focus of these assessments will vary based on individual circumstances and exposure sources other than lead paint hazards should be considered before conducting environmental testing.

Environmental assessments in housing built in 1978 or after should include:

- History of child's exposure and questionnaire on potential sources of exposure;
- Visual inspection of the home and any other facility where the child spends considerable time to identify potential exposure sources and other relevant conditions;
- Environmental sampling if conditions suggest that potential lead sources are present (e.g. water, soil, dust).

In addition, environmental assessments may include investigation of potential exposures from other sources including, but not limited to, toys and other products, pottery cosmetics, folk remedies, food and candy with significant lead content. The potential for take home exposures must also be evaluated based on the parent's occupation and hobbies. In some subpopulations such as immigrants, imported products, foods, and folk remedies may be more commonly found and therefore a more substantial contributor to lead exposures among children than in other communities.

Recommendations

Although the long-term goal is to eliminate lead hazards in housing and child occupied environments, it is clear that this aspiration cannot be achieved overnight. Many environmental assessments in housing are still going to be triggered by the presence of a child with a BLL that exceeds a defined threshold. Any venous BLL that is above the reference value for children should trigger an environmental investigation to evaluate potential sources of exposure.

Any individual exposure that is significantly above the reference value suggests that one or more source or pathway of exposure exists in the child's environment that requires exposure reduction. Exposures to lead hazards in homes or other child occupied facilities significantly contribute to children's BLLs above the reference value. These hazards include lead levels above EPA guidelines and/or regulations covering dust, soil, drinking water, and the presence of deteriorated paint above specified quantities.

In situations where any lead hazards are present, the results of the environmental investigation should be used to prioritize and plan hazard controls to reduce exposures. Hazard control options should be developed by licensed or certified lead-based paint risk assessors and

should be performed based on documented guidance and regulations ([78]; <http://portal.hud.gov/hudportal/HUD?src=/program_offices/healthy_homes/lbp/hudguidelines). If environmental investigations uncover lead hazards triggering a response in a single unit in multi-family housing, the response action should be applied to all similar untested units within the housing development, unless a risk assessment shows that the other units are free of lead hazards.

VI. Research Needs

KEY POINTS/RECOMMENDATIONS

- ***CDC should encourage additional research directed towards developing interventions capable of maintaining children's BLLs below the reference value.***
- ***Additional research priorities should include efforts to improve the use of data from screening programs, develop next generation point-of-care lead analyzers, and improve the understanding of epigenetic mechanisms of lead action.***

Evaluation of interventions to reduce exposure

It is axiomatic that reduction of exposure to lead will prevent the consequences of exposure. In many cases, interventions to reduce exposure will require little or no evaluation, and can be implemented with the full expectation that they will work. Preventing the importation of lead-painted toys and children's jewelry, for example, should reduce or prevent exposure from that source. Less clear, however, is the efficacy of specific interventions to keep blood lead concentrations below the reference value in children living in pre-1978 housing. Funding agencies should seek out and support work to develop and evaluate effective, broadly useful interventions that work in the complex exposure situations that are commonly encountered. In addition, when primary prevention programs are implemented, program officials should establish ways of measuring their effectiveness.

Secondary Prevention

Evidence that nutritional interventions affect BLLs is limited. However, higher dietary calcium, iron, vitamin C, and zinc have been associated with lower blood lead concentrations at least in infancy [83][84]. Calcium, zinc, and vitamin C are thus worth further investigation. Iron deficiency and higher BLLs can occur in the same children and may have similar consequences [23]; children exposed to lead should be evaluated for anemia and iron deficiency according to current AAP guidelines [57], and any deficiency corrected. AAP does state that, although correction of iron deficiency may also reduce the absorption of lead, that "iron supplementation in a child with iron deficiency anemia who also has lead poisoning without chelation therapy seems to increase blood lead concentrations and decrease basal lead excretion." This situation is rare, and the effect was seen in only one study [85] in children with BLLs >25 μg/dL. The ACCLPP recommends that research to clarify this specific situation be supported, but that lead-exposed children with BLLs <25 μg/dL be treated the same as any other children as far as iron is concerned.

Children with cognitive or behavioral problems associated with lead exposure would benefit from interventions that improve academic performance in children such as those participating in Head Start. The ACCLPP has charged another Work Group to recommend strategies on the educational needs of children with elevated BLLs. Because lead exerts long-lasting effects and the effect of lead on a child may not be demonstrable until the child is well into the elementary school years, this report appropriately focuses recommendations for educational needs across the age span of infancy through 21 years. The document will include a consideration of research needs specific to this area.

Sources and routes of exposure in older children

Blood lead concentrations are lower in older children, but most studies find a stronger association between blood lead and IQ for the concurrent blood lead measurements, than for a child's peak blood lead at age 2 years. Although much is known about behavior and exposure in toddlers, older children have not been extensively studied and how they are exposed is less well understood. Older children are more mobile, the scale of their environment is larger, and the sources and routes of exposure likely differ from those for younger children. A systematic analysis of what is already known for older children could provide a sound rationale for the design of additional research on exposure pathways in these children. Research into the various lead suspension, transport, and redeposition mechanisms at the neighborhood level, and how these impact lead exposures is needed. Also additional research into urban lead remediation done throughout a neighborhood, rather than on an individual property basis, could add to our understanding of exposure reduction among children with relatively low level exposures.

Research on other uses of the results from screening programs

Although NHANES is a large, ongoing U.S. survey that currently includes children's BLLs, it does not provide prevalence estimates for elevated BLLs for any segment smaller than a multi-state region. Individual states and cities often have screening data, but it is not population-based. The relationship between distribution of BLLs in the population and in a screened sample can vary, and findings from NHANES and state lead programs should be viewed as complementary. Population-based estimates of BLLs ≥10μg/dL in high risk neighborhoods in Chicago were similar to those calculated using surveillance data collected by the health department [86].

As the number of children tested and reported to CDC increases, the NHANES and national surveillance estimates become closer. The percent of children with BLLs ≥ 10 μg/dL reported to CDC

decreased from 7.6% in 1997 to 3.1% in 2001, close to the NHANES estimate of 2.2% for 1999-2000 [87]. In 2008, among the children tested for lead and reported to CDC, 0.83% were ≥ 10 µg/dL. The 2007-2008 NHANES estimate for BLLs ≥ 10 µg/dl was 1.22%, although this estimate is statistically unstable. (CDC, unpublished data) These instances raise the possibility that a predictable relation exists between the two methods. Since population-based surveys are difficult to conduct, it would be helpful to have additional comparisons between surveillance programs (screening) and population-based survey data to see if there are reliable associations between them. If there are, this would be helpful both for prioritizing prevention activities and assessing progress at the state and local level.

Better point-of-care lead analyzers

Given the present focus on lower BLLs, development of new point-of-care (POC) lead analyzers with better sensitivity, as well as increased accuracy and precision (e.g. +/- 1 µg/dL) at BLLs <5 µg/dL would be desirable. Current POC lead analyzers appear to provide their optimal performance at around the 10 µg/dL. It is at higher BLLs where POC lead analyzers performance is relatively poorer. Beyond that, developing new analytical approaches based on improved electrochemistry, use of novel plasma on a chip technology, non-destructive techniques based on MµXRF, or other portable multi-elemental analyzers that would include other hazardous elements might meet the needs of both the clinical and the research communities.

Epigenetic mechanism of lead action

A promising new area of research suggests that epigenetic mechanisms may play a role in how early life exposure to lead influences development of the brain and other organ systems. These alterations involve chemical modifications to the DNA, or regions surrounding the DNA, but do not

involve mutations to the DNA sequence itself. Such alterations can influence patterns of gene expression, and can persist even in the absence of continued exposure to lead. Epigenetic changes, in the appropriate context, also have the potential for transgenerational inheritance [88-91]. Such changes have been linked to elevated BLLs in human cohorts [92]. It will be critical to understand how lead modifies epigenetic profiles, particularly since some of these alterations appear to be labile and thus could be mitigated through subsequent behavioral experiences or other interventions. Studies examining such relationships would further our understanding of how behavioral, academic, or other interventions could be used to attenuate lead-related adverse health effects.

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